

Recurrent Miscarriages in Advance Maternal Age (>35 Years)

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ABSTRACT

Objective: To determine frequency of recurrent miscarriages in advance maternal age (>35 years).

Study Desing: Descriptive cross-sectional study.

Place and Duration of the Study: Department of Obstetrics and Gynaecology, Bakhtawar Amin Trust Teaching Hospital, Multan, Pakistan, from January 2021 to June 2021.

Material and Methods: One hundred and ninety six women were enrolled. The demographic information like name, age, address, number of gravida, para and the number of miscarriages was obtained. The outcome variable (proportion of woman having recurrent miscarriages) was recorded on a specific proforma. Descriptive statistics were applied to analyze the data.

Results: Among 196 women, 122 (62.2%) were aged between 35 to 40 years. Overall mean age was calculated to be 38.1±3.6 years. Analysis of gravidity and parity distribution showed that majority of women, 55 (28.1%) were G6P1A4 while G5P1A3 were 41 (20.9%). There were 86 (43.9%) women who had conceived 6 times in the past. Among 196 women with recurrent miscarriages, majority of the patients 109 (55.6%) were having previous 3 miscarriages. Frequency of recurrent miscarriages in maternal age >35 years in the present study was found to be 14.8%

Conclusion: Increased risk of fetal loss was observed with increasing maternal age in women aged more than 35 years. Frequency of recurrent miscarriages in advance maternal age was 14.8%.

Keywords: Recurrent miscarriages, maternal age, fetal loss.

INTRODUCTION

Recurrent miscarriage refers to the loss of three or more consecutive pregnancies before the age of viability.¹ Miscarriages affect between 1-2% women.² Advanced maternal is described as age above 35 years at the estimated time of delivery.³ Large prospective trials have shown age linked risk of miscarriage as 13% in women aged between 12 to 19 years, 11% in 20 to 24 years, 12% in 25 to 29 years, 15% in 30 to 34 years, 25% in 35 to 39 years, 51% in 40 to 44 years and 93% in more than 45 years.⁴ This might be due to decline in both number and quality of oocytes.⁵ Couples who have had a pregnancy loss have two concerns, the cause and the risk of recurrence. Chances of miscarriage enhance with every successive pregnancy loss and reaches around 40% following 3 consecutive pregnancy losses.^{4,5}

Age and previous pregnancy outcome are two independent risk factors of recurrent pregnancy losses.⁶ Structural chromosomal abnormality occurs in approximately 3% of cytogenetically abnormal abortuses and these most commonly are inherited from mother.⁷ Proposed causes of recurrent miscarriages include parental and fetal chromosomal abnormalities, structural uterine abnormalities, autoimmune diseases and endocrinological disorders. The rate of normal euploid and aneuploid abortuses increase with maternal age.^{8,9} In a comparative study conducted at Baqai Hospital, Karachi, Pakistan showed that recurrent miscarriage is the most detected complication in advanced maternal age, 18.6% in more than 35 years versus 12% in age less than 30 years.¹⁰

Nishtar hospital is one of the major institutions catering services to the gynaecological and obstetrical patients in Southern Punjab. Many patients with the complaint of recurrent miscarriages are brought to the Nishtar Hospital Multan. We wanted to know the frequency of recurrent miscarriages in pregnant women with advanced maternal age as no such study had been done earlier in this region. This will highlight the couples at risk and will help in reducing its incidence through timely evaluation, pregestational diagnosis and managing these patients according to the standard protocols.

MATERIAL AND METHODS

This descriptive cross-sectional study was done at "The Department of Obstetrics and Gynaecology Bakhtawar Amin Trust

Teaching Hospital, Multan, Pakistan", from January 2021 to June 2021. Informed written consent was sought from all women. Ethical clearance was acquired from the Institution.

A sample size of 196 women was calculated using formula:

$$n = \frac{(Z_{1-\alpha/2})^2 \times P(1-P)}{d^2}$$

$$Z = 1.96$$

P (Expected prevalence) = 18.6% prevalence of miscarriages¹⁰

Absolute precision required = $d = 5.5\%$,

A total of 196 multigravida (conceived > 3 times) women aged >35 years with gestational age < 20 weeks were enrolled. All women who had induced miscarriage, ectopic pregnancy, molar pregnancy, biochemical pregnancy and miscarriages due to other known causes i.e. endocrine disorders, uterine anomalies, autoimmune disorders, and coagulation disorders were not included. Miscarriage was labeled as loss of pregnancy before 20 weeks of gestation or of fetus less than 500 grams.¹ Recurrent miscarriage was defined as loss of three or more consecutive spontaneous losses of pregnancies before 20 weeks of gestation or of fetus <500 grams.¹ Advanced maternal age was labeled when the age was more than 35 years

The demographic information like name, age, address, number of gravida, para and the number of miscarriages were obtained. The maternal age at the time of each pregnancy demise was determined. If there was a twin gestation, the miscarriage was considered as a single event. The retrospective information about prior pregnancy losses was obtained, if index and/or prior miscarriages are three or more, these women were considered as patients of recurrent miscarriages. The outcome variable (proportion of woman having recurrent miscarriages) was recorded on a specific proforma. The same protocol and questionnaire was applied to all members of the cohort by the researcher.

Data was analysed with SPSS 26.0. Quantitative data was shown as mean and standard deviation while qualitative variables were expressed as frequency and percentage. Chi square test was applied post stratification and P value less than 0.05 was considered significant.

RESULTS

Among 196 women, 122 (62.2%) were aged between 35 to 40 years. Overall mean age was calculated to be 38.1±3.6 years. Analysis of gravidity and parity distribution showed that majority of women, 55 (28.1%) were G6P1A4 while G5P1A3 were 41 (20.9%). There were 86 (43.9%) women who had conceived 6 times in the past. Among 196 women with recurrent miscarriages, majority of the patients 109 (55.6%) were having previous 3 miscarriages. Table 1 is showing distribution of characteristics of all the women.

Table 1: Characteristics of Women (n=196)

Characteristics		Number (%)
Age (years)	35-40	122 (62.2%)
	41-45	66 (33.7%)
	>45	8 (4.1%)
Gravidity and Parity Status	G4P0A3	37 (18.9%)
	G5P1A3	41 (20.9%)
	G6P2A3	31 (15.8%)
	G6P1A4	55 (28.1%)
	G7P1A5	32 (16.3%)
History of Number of Conceptions	4	37 (18.9%)
	5	41 (20.9%)
	6	86 (43.9%)
	7	32 (16.3%)
Number of Previous Miscarriages	3	109 (55.6%)
	4	55 (28.1%)
	5	32 (16.3%)

Figure 1 is showing that the frequency of recurrent miscarriages in maternal age >35 years in the present study was found to be 14.8%

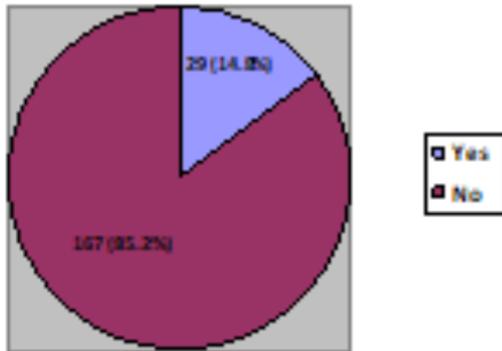


Figure 1: Frequency of recurrent miscarriages in maternal age >35 years

Table 2 is showing stratification of recurrent miscarriages according to age and number of conceptions. No statistically significant difference was noted among women with regards to recurrent miscarriage in the present study (p>0.05).

Table 2: Stratification of Recurrent Miscarriages according to Age and Number of conceptions (n=196)

Study Variables	Recurrent miscarriage		P value
	Yes (n=29)	No (n=167)	
Age (years)	35-40	18	0.9800
	41-45	10	
	>45	1	
Number of conceptions	4	5	0.9948
	5	6	
	6	13	
	7	5	

DISCUSSION

Many maternal factors are linked with recurrent miscarriage. Increasing aging has been labeled as one of the major risk factors responsible for the increased risk of recurrent miscarriages.^{11,12}

After 35 years of age, the risk of miscarriage rises swiftly and it is around 75% among women aged above 45 years.⁴ Possible explanation behind increased chances of miscarriage in the advanced maternal age could be the relationship of maternal age and chromosomal abnormalities in the fetus.⁸ Advanced maternal age is also known to degrade ovarian functioning while decline in number of quality oocytes is also reported in these women. Many researchers have reported increased chances of fetal mortality and spontaneous abortions with increasing maternal age.¹³ Factors like past history of spontaneous abortions and multigravidity have also been linked with recurrent miscarriages in the past.^{14,15}

In the present study, we found that 55.6% women had experienced 3 miscarriages in the past. Ogasawara M and colleagues reported risk of miscarriage to be 44%, 45% and 62% among women who had history of 2, 3 and 4 miscarriages respectively.¹⁶ Local data has revealed 71.8% cases of recurrent miscarriages to be with 3 to 4 previous miscarriages.¹⁷ In the present study, 55.6% women were having 3 miscarriages in the past. In an International study, mean miscarriage in studies population was 2.28±1.49 (ranging between 0-6).¹⁸

In the present study, frequency of recurrent miscarriages in maternal age >35 years was 14.8%. A recent study from Norway revealed that risk of miscarriage was highest among women aged above 45 years (53.6%) while it was lowest among women aged between 25 to 30 years (9.8%).¹⁹ Another population based study from Denmark exhibited that chances of miscarriage were highest among women who were in their late 30s.⁴

Researchers have shown that the risk of miscarriage is as low as 5% among young women with no history of miscarriages but increased maternal age puts women at significantly increased risk of recurrent miscarriage and there must be underlying causes.²¹ Increasing rate of pregnancy loss were reported from 2.1% at less than 30 years to 20% in women over 40 years of age.²² The profound impact of maternal age on pregnancy outcome is similarly demonstrated in another study.²³

This study had some limitations as well. As this was a single center study, our findings cannot be generalized. More population based studies involving multiple centers and large sets of women with recurrent miscarriages should be planned to find out the exact burden and causes behind recurrent miscarriages in advanced maternal age. We were unable to follow up women in subsequent fertility outcomes so longitudinal prospective studies should also be planned to enlighten us about various aspects of recurrent miscarriages among women with advanced maternal age in the local population.

CONCLUSION

Increased risk of fetal loss was observed with increasing maternal age in women aged more than 35 years. Frequency of recurrent miscarriages in advance maternal age was 14.8%.

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